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EXAMINER	
LAM, ANN Y	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,292	HATTORI ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 10-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *11-14* is/are allowed.

6)☒ Claim(s) *1-7,10, 15-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 10 and 20-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al., 6,235,471, in view of Prince et al., WO 98/13131.

Knapp et al. teach microfluidic devices that include chambers and channels, fluidly connected to allow transport of fluid among the chambers and/or channels of these devices. Knapp et al. also disclose that "fluidly connected" refers to a junction between two regions, e.g., chambers, channels, wells etc., through which fluid freely passes. Such junctions may include ports or channels which can be clear, i.e., unobstructed, or can optionally include valves, filters, and the like, provided that fluid freely passes through the junction when desired. See column 42, lines 12-35.

As to claims 1, 7 and 20, the filter is equivalent to the claimed permeation limiting zone that is capable of limiting permeation of at least a part of particles flowing in a liquid [i.e., particles larger than the openings of the filter]. It is noted that "where one or more second channels are branched out from said first channel" reads on a channel that is continuous, wherein the portion on one side of the filter is considered to be one

channel and the portion on the other side of the filter is considered to be a second channel. Alternatively, it would have been obvious to one of skill in the art from the disclosure regarding a junction between two regions, e.g., chambers, channels, wells etc., that a junction can include a junction between two channels such that they form a T or Y junction, as such shaped junctions are well known.

However, Knapp et al. do not specify details regarding the filter. Thus Knapp et al. do not specifically disclose the claimed limitation regarding the filter being a plate-formed partition wall having a plurality of openings formed from circles, ovals, polygonal holes or slits.

However, Prince et al. teach filter membranes which are disclosed as capable of being employed in many different filtration systems, including cross flow filtration (page 22, lines 31-35.) Prince et al. teach that the shape and size of the pores and the spacing between the pores may be selected depending on the desired application (page 13, lines 35-37.) Specifically, Prince et al. disclose a membrane filter with pores having precisely dimensioned shapes and sizes corresponding to the shape of the particles to allow their passage but to block passage of a second type of particle. The device is disclosed as being useful for the separation of cells, cell components or fragments of cells, and the various blood components may be used for diagnostic or therapeutic purposes. (page 7.) Prince et al. teach that for example if it is desired to separate white blood cells from red blood cells, a filter membrane may be provided that has pores precisely rectangularly dimensioned to measure approximately 1.8 microns to 3.5 microns by approximately 6.0 microns to 14.0 microns to allow passage of red blood

cells without deformation or with only minor deformation, and white blood cells only upon substantial deformation. The whole blood and filter membrane are brought into contact with a sufficient time and/or sufficient force to allow passage of red blood cells but insufficient for passage of white blood cells (pages 10-11 and figure 4.)

The Prince et al. filter is equivalent to the claimed permeation limiting zone having a plate-formed partition wall having a plurality of openings formed from circles, ovals, polygonal holes or slits [e.g., rectangular openings.] Because the type of filter in the Knapp et al. invention is not limited to any particular type, the skilled artisan would thus look to the art, such as the Prince et al. reference, for specific types of filter as would be appropriate for filtering out the desired materials in the Knapp et al. device. Therefore use of the Prince et al. filter in the Knapp et al. invention would have been within the skills of the ordinary artisan.

As to claim 2, there is inherently a plurality of obstacles arranged as being spaced from each other (i.e., forming openings.) (It is noted that one contiguous element can be considered to be comprised of obstacles arranged as being spaced from each other.

As to claim 3, the filter allows only a part [portion] of the particles in the liquid to permeate through a gap between adjacent obstacles, i.e., particles that are larger than the gap.

As to claim 4, because Knapp et al. do not disclose the specific details regarding the filter, Knapp et al. also do not disclose that the direction of force causing flow of the particles lies non-parallel with direction of arrangement of the obstacles at the front-

most plane on the filter at the front-most plane on the branching point side of the filter. However, providing a filter membrane, such as that taught by Prince et al., perpendicular, i.e., non-parallel, to the fluid flow direction is well known in the art as such configuration will serve to filter out the desired materials.

As to claim 5, the filter will guide at least a part [portion] of the particles to either the first channel or second channel, depending on the arrangement thereof, [and depending on the size of the particles relative to the size of the openings of the filter.

As to claim 6 the obstacles are inherently formed in a two-dimensional manner. The term "periodically arranged" relates to method of manufacturing, and since the claim is directed to a device, the prior art only needs to disclose the same structural elements.

As to claim 10, Knapp et al. do not disclose that a gap between the adjacent obstacles of the filter in the direction of formation of the main channel differs from that in the direction of formation of the side channel. However, as noted above, a T or Y junction is a well known configuration, and providing a filter in one of the channels at such junctions, as suggested by the teachings of Knapp et al. as discussed above, would result in a filter having the claimed limitations of claim 10.

As to claim 20, the Knapp et al. microfluidic device is equivalent to a chip.

As to claim 21, Knapp et al. disclose that the substrate typically includes a detection window or zone at which a signal is monitored. This detection window typically includes a transparent cover allowing visual or optical observation and detection of the assay results. Example detectors include spectrophotometers,

photodiodes, microscopes, scintillation counters, cameras, etc. and examples of suitable detectors are widely available from a variety of commercial sources known to persons of skill. See column 53, lines 40-53.

As to claim 22, Knapp et al. disclose that the substrate typically includes a detection window or zone at which a signal is monitored. This detection window typically includes a transparent cover allowing visual or optical observation and detection of the assay results. Example detectors include spectrophotometers, photodiodes, microscopes, scintillation counters, cameras, etc. and examples of suitable detectors are widely available from a variety of commercial sources known to persons of skill. See column 53, lines 40-53. Knapp et al. also disclose in the background section of the patent, that mass spectrometry is also another detection techniques known in the art of microfluidics. See column 1, lines 27-38. However, Knapp et al. do not specifically list mass spectrometry as one of the detection techniques that may also be used in combination with the microfluidic device disclose. The skilled artisan however would recognize that mass spectrometry may also be incorporated into the disclosed microfluidics, since it is a well known detection technique in the art, as discussed in the background section.

As to claims 23-24, Knapp et al. disclose that the device includes a size separation zone for separating products by size. In one embodiment, the apparatus will include a substrate such as a membrane having, e.g., 4,096 spots (i.e., all possible 6-mer primers). Knapp et al. state that similarly, components in diagnostic or drug screening assays can be stored in the well or membrane format for introduction into the

analysis region of the device, and that arrays of nucleic acids, proteins and other compounds are also used in a similar manner. See column 7, line 45 to column 8, line 16. Thus Knapp et al. teach a screening assay by binding proteins to membrane spots or providing a separation zone for proteins.

As to claim 25, Knapp et al. do not disclose a method of using the device to detect separated proteins that are decomposed by protease treatment. However, Knapp et al. teach that because of the breadth of the available sample storage formats for use with the present invention, virtually any set of reagents can be sampled and assayed in an integrated system of the present invention. For example, enzymes and substrates, receptors and ligands, antibodies and ligands, proteins and inhibitors, immunochemicals and immunoglobulins, proteins, etc., can all be assayed using the integrated systems disclosed. See column 31, lines 3-20. Separating proteins decomposed by protease treatment is well known in the art and utilizing the Knapp et al. device to provide the assay steps, including identification, is suggested by Knapp et al.

As to claim 26, the Knapp et al. microfluidic device is a chip. Also, using affinity to capture target proteins using the Knapp et al. microfluidic device is disclosed (see column 37, lines 8-25 disclosing solid phase reagent interface using capture elements; and see col. 28, lines 48-50 disclosing antibody-antigen binding as examples of types of assays that can be performed using the device.)

As to claim 27, washing the surface where molecules have been captured is well known in the art to remove unbound material.

As to claims 28-30, Applicant claims that a particle satisfying an angle between 0 to 90 degrees to the obstacles never clog gaps in the obstacles. It is noted that the claims at issue are directed to an apparatus, and this language thus relates to intended use. As discussed in claim 1 above, use of a T junction is well known in the art, and given the teachings of Knapp et al. to provide a filter at a junction, it is well within the skills of the ordinary artisan to provide a filter at the T junction, such as at the side channel, where the force of fluid flow is parallel to the filter (i.e., 0 degrees to the obstacles of the filter). There is no specification as to the size of the particles in the claims. Thus, such a filter as mentioned is capable of not clogging in the gaps of the obstacles of the filter, particularly where in use the particles are larger than the gaps and especially where the force of fluid flow is parallel to the filter.

Claims 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al., 6,235,471, in view of Prince et al., WO 98/13131, and further in view of Sundberg et al., .6,086,825.

The disclosures of Knapp et al. and Prince et al. have been discussed above. Additionally, Knapp et al. disclose that the microfluidic device has a material transport system for controllably transporting a material through and among the reagent introduction channel and reaction channel. For example, the material transport system can include electrokinetic, electroosmotic, electrophoretic or other fluid manipulation

aspects (micro-pumps and microvalves, fluid switches, fluid gates, etc.) which permit controlled movement and mixing of fluids. See column 5, lines 4-39. (The electrokinetic transport system comprises the claimed first drive means for migration speed in one direction and a second drive means for migration speed in a different direction since differently charged particles will move in different directions.).

However, Knapp et al. do not disclose a width of entrance to the filter to be narrower than the width of the filter zone.

Sundberg et al. however disclose microfluidic substrates having channels varying in cross-sectional dimension so that capillary action spreads a fluid only within a limited portion of the channel network. In another aspect, the introduction ports may include a multiplicity of very small channels leading from the port to a fluid channel, so as to filter out particles or other contaminants which might otherwise block the channel at the junction between the channel and the introduction port. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide a width of entrance to the filter that is narrower than the width of the filter zone as may be desired as disclosed by Sundberg et al. for purposes such as limiting the spread of capillary action or blocking contaminants.

As to claims 16-17, the types of particles is not recited as part of the claimed device and relates to intended use. The Knapp et al. filter is capable of filtering the recited particles, depending on the size of the particles.

As to claim 18, the Knapp et al. micro-pumps or microvalves are capable of functioning to introduce a suspension of particles and diluting the suspension [with a fluid].

As to claim 19, the step of desalting is a method step and the claims are directed to a device rather than a method. The Knapp et al. device is capable of desalting the suspension since it has micro-pumps and microvalves for introducing a desalting medium.

Allowable Subject Matter

Claims 11-14 are allowed.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. O'Connor et al. 6,729,352, disclose that a filter in a microfluidic device can be porous beads or a mesh, for trapping materials in a fluid (column 16, lines 30-44.) It is noted that a mesh can be considered to be comprising a plurality of columns (e.g. cylinders.)

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641